STRUCTURE FILE UPDATES: 19 SEP 2005 HIGHEST RN 863478-08-4
DICTIONARY FILE UPDATES: 19 SEP 2005 HIGHEST RN 863478-08-4

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

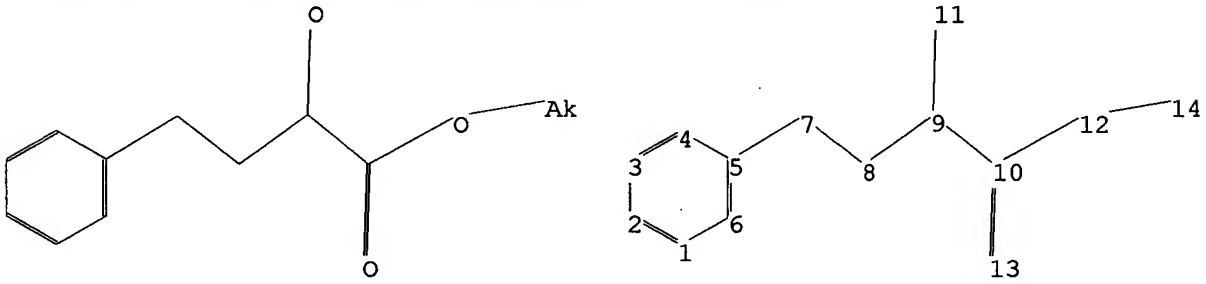
Please note that search-term pricing does apply when
conducting SmartSELECT searches.

****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS
for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\10719660.str



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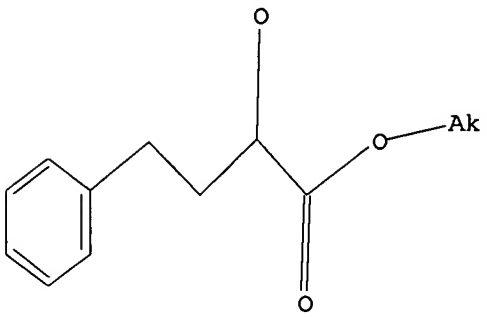
7 8 9 10 11 12 13 14
ring nodes :
1 2 3 4 5 6
chain bonds :
5-7 7-8 8-9 9-10 9-11 10-12 10-13 12-14
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
9-11 10-12 10-13 12-14
exact bonds :
5-7 7-8 8-9 9-10
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SEARCH INITIATED 16:16:38 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 2151 TO ITERATE

93.0% PROCESSED 2000 ITERATIONS 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 40238 TO 45802
PROJECTED ANSWERS: 653 TO 1541

L2 50 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 16:16:43 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 43191 TO ITERATE

100.0% PROCESSED 43191 ITERATIONS 1314 ANSWERS
SEARCH TIME: 00.00.01

L3 1314 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 161.33 161.54

FILE 'CAPLUS' ENTERED AT 16:17:09 ON 20 SEP 2005
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FILE COVERS 1907 - 20 Sep 2005 VOL 143 ISS 13
FILE LAST UPDATED: 19 Sep 2005 (20050919/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> s l3/p
L4          671 L3/P

=> s l3 and (process or make or made or synthes? or method)
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        1436157 PROCESSES
        3194259 PROCESS
                  (PROCESS OR PROCESSES)
         216040 MAKE
         168027 MAKES
         372909 MAKE
                  (MAKE OR MAKES)
        1166867 MADE
             24 MADES
        1166888 MADE
                  (MADE OR MADES)
        1476331 SYNTHES?
        2940330 METHOD
        1210143 METHODS
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L5          446 L3 AND (PROCESS OR MAKE OR MADE OR SYNTHES? OR METHOD)

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          70084 NITRILE
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        4035727 ACID
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                  (ACID OR ACIDS)
L6            4 L5 AND (NITRILE AND ACID)

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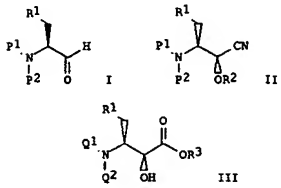
L6 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:700272 CAPLUS
DOCUMENT NUMBER: 141:174475
TITLE: Process for producing erythro-3-amino-2-hydroxybutyric acid derivatives
INVENTOR(S): Furukawa, Yoshiro; Yaegashi, Keisuke; Hinoue, Kazumasa
PATENT ASSIGNEE(S): Daiso Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1449824	A1	20040825	EP 2004-290653	20000622
R: CH, DE, FR, GB, LI				
EP 1063232	A2	20001227	EP 2000-401792	20000622
EP 1063232	A3	20010307		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: JP 1999-174967 A 19990622
EP 2000-401792 A3 20000622
OTHER SOURCE(S): CASREACT 141:174475; MARPAT 141:174475
GI

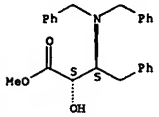


AB A process for producing an erythro-3-amino-2-hydroxybutyric acid derivative involves reaction of a 2-amino aldehyde derivative I [R1 is alkyl, cycloalkyl, alkylthio, arylthio or (un)substituted aryl; P1, P2 are (un)substituted aralkyl, alkyloxycarbonyl, arylcarbonyl or arylsulfonyl] with a metal cyanide in the presence of an acid chloride and/or an acid anhydride to give stereoselectively an erythro-3-amino-2-hydroxybutyronitrile derivative II [same R1, P1 and P2; R2 is alkylcarbonyl or (un)substituted arylcarbonyl group]. The nitrile derivative II is treated with an acid in water or aqueous solvent to convert it into an erythro-3-amino-2-hydroxybutyric acid derivative III [same R1; R3 is H; Q1, Q2 are H, (un)substituted aralkyl or arylsulfonyl] or with an acid in an alc. solvent R3OH to convert it into an ester III [same R1, Q1 and Q2; R3 is alkyl, cycloalkyl or (un)substituted aralkyl] under two-phase catalysis. Thus, the process was applied to the synthesis of Me (2S,3S)-3-(dibenzylamino)-2-hydroxy-4-phenylbutyrate (erythro:threo = 87:13, 73% yield) starting from N,N-dibenzyl-L-phenylalaninal.

L6 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

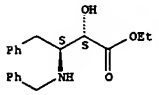
IT 189562-45-6P 313468-87-0P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(production of aminohydroxybutyric acid derivs.)
RN 189562-45-6 CAPLUS
CN Benzenebutanoic acid, β-[bis(phenylmethyl)amino]-α-hydroxy-, methyl ester, (αS,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 313468-87-0 CAPLUS
CN Benzenebutanoic acid, α-hydroxy-β-[(phenylmethyl)amino]-, ethyl ester, (αS,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1993:560824 CAPLUS
DOCUMENT NUMBER: 119:160824
TITLE: Process for the preparation of α-hydroxy-β-aminocarboxylic acids
INVENTOR(S): Baenziger, Markus; Warm, Aleksander; McGarrity, John
PATENT ASSIGNEE(S): Lonza A.-G., Switz.
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

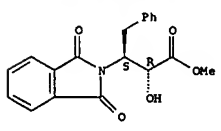
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 543343	A2	19930526	EP 1992-119634	19921117
EP 543343	A3	19930721		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
JP 06184069	A2	19940705	JP 1992-303629	19921113
CA 2083108	AA	19930520	CA 1992-2083108	19921117

PRIORITY APPLN. INFO.: CH 1991-3373 A 19911119
OTHER SOURCE(S): CASREACT 119:160824; MARPAT 119:160824

AB R1CH(NR3R4)CH(OH)CO2R2 [R1 = (substituted) alkyl; R2 = H, alkyl; R3, R4 = H, protecting group; R3R4 = bifunctional protecting group], were prepared by 1) treatment of R1CH(NR5R6)COX (R5,R6 = R3,R4, except that both R5,R6 cannot = H; X = Br, Cl) with Me3SiCN to give R1CH(NR5R6)COCN, 2) conversion of the nitrile to R1CH(NR5R6)COCO2R7 (R7 = alkyl), 3) selective reduction of the keto group, and 4) optional deprotection/ester hydrolysis. Thus, N-phthaloyl-L-phenylalanine was refluxed with SOCl2 to give 98% acid chloride, which was heated with Me3SICN and ZnI2 in THF to give 87% nitrile. This in Et2O/MeOH/HCl was stirred at -10° followed by addition of H2O to give 68% Me S-2-oxo-4-phenyl-3-phthalimidobutyrate. The latter was reduced with LiBH4 in THF at -25° to give 96% Me (2R,3S)- and (2S,3S)-2-hydroxy-4-phenyl-3-phthalimidobutyrate. This was converted to cyclohexylnorstatine hydrochloride.

IT 150095-77-5P 150095-78-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for α-hydroxy-β-aminocarboxylic acid derivative)
RN 150095-77-5 CAPLUS
CN 2H-Isoindole-2-propanoic acid, 1,3-dihydro-α-hydroxy-1,3-dioxo-β-(phenylmethyl)-, methyl ester, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

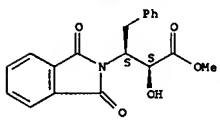
Absolute stereochemistry.



RN 150095-78-6 CAPLUS
CN 2H-Isoindole-2-propanoic acid, 1,3-dihydro-α-hydroxy-1,3-dioxo-β-(phenylmethyl)-, methyl ester, (αS,βS)- (9CI) (CA INDEX NAME)

L6 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

Absolute stereochemistry.



L6 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

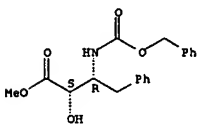
ACCESSION NUMBER: 1992:651744 CAPLUS
DOCUMENT NUMBER: 117:251744
TITLE: Aminodeoxybestatin and epi-aminodeoxybestatin: stereospecific synthesis and aminopeptidase inhibition
AUTHOR(S): Herranz, Rosario; Vinuesa, Soledad; Castro-Pichel, Julia; Perez, Concepcion; Garcia-Lopez, M. Teresa
CORPORATE SOURCE: Inst. Quim. Med., CSIC, Madrid, 28006, Spain
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1992), (14), 1825-30
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 117:251744

AB The synthesis of (2S,3R)-DAPBA-L-Leu-OH (DAPBA = 2,3-diamino-4-phenylbutanoic acid) (aminodeoxybestatin) and (2R,3R)-DAPBA-L-Leu-OH (epi-aminodeoxybestatin), bestatin and epi-bestatin analogs, resp., in which the hydroxy group has been replaced with an amino group, is described by two different methods. The first one involves the synthesis of bis-(N-Z)-DAPBA (Z = benzyloxycarbonyl), by homologation of N-Z-phenylalanine, via a modified Strecker synthesis followed by subsequent coupling with the Me ester of L-leucine and removal of the protecting groups. Following this procedure, 25% racemization at the C-3 center of the DAPBA derivs. took place during the homologation reaction. The second method involves the stereospecific SN2 nucleophilic substitution of the 2-hydroxy group of (2R,3R)- and (2S,3R)-3-(benzyloxycarbonyl)amino-2-hydroxy-4-phenylbutanoyl-L-leucine Me esters, and subsequent saponification, azido reduction and removal of the N-Z-protecting group. Replacement of the hydroxy group of bestatin and epi-bestatin with an amino group results in a decrease in their aminopeptidase (AP-B, AP-M and Leu-AP)-inhibitory potencies.

IT **124782-04-3P 124782-06-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and mesylation of)

RN 124782-04-3 CAPLUS
CN Benzenebutanoic acid, α-hydroxy-β-[[(phenylmethoxy)carbonyl]amino]-, methyl ester, (αS,βR)- (9CI) (CA INDEX NAME)

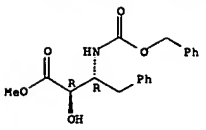
Absolute stereochemistry. Rotation (+).



RN 124782-06-5 CAPLUS
CN Benzenebutanoic acid, α-hydroxy-β-[[(phenylmethoxy)carbonyl]amino]-, methyl ester, (αR,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

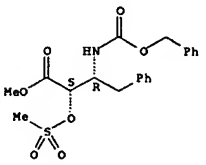
L6 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



IT **144676-50-6P 144676-51-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and substitution reaction of, with azide)

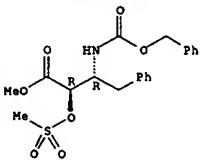
RN 144676-50-6 CAPLUS
CN Benzenebutanoic acid, α-[(methylsulfonyl)oxy]-β-[[(phenylmethoxy)carbonyl]amino]-, methyl ester, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 144676-51-7 CAPLUS
CN Benzenebutanoic acid, α-[(methylsulfonyl)oxy]-β-[[(phenylmethoxy)carbonyl]amino]-, methyl ester, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1957:1600 CAPLUS
DOCUMENT NUMBER: 51:1600
ORIGINAL REFERENCE NO.: 51:287d-i,288a-b
TITLE: The synthesis of mandelic acid analogs. II. Styrylglycolic acids
AUTHOR(S): Nerdel, Friedrich; Rachel, Hans
CORPORATE SOURCE: Tech. Univ., Berlin-Charlottenburg
SOURCE: Chemische Berichte (1956), 89, 671-7
CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 51:1600

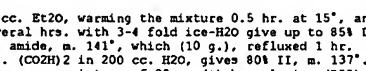
AB cf. C.A. 49, 6217e. Adding dropwise 54 cc. concentrated HCl to 80 cc. PhCH:CHCHO and 49 g. NaCN in 250 cc. Et2O cooled with ice, stirring the mixture 1 hr. at 0° and 1 hr. at 20°, washing the filtered Et2O solution with concentrated NaHSO3 and recrystg. the residue from CS2 give 65-70% DL-PhCH:CHCH(OH)CN (I), m. 74-5°. Adding dropwise at below 10° a mixture of 250 cc. concentrated HCl and 40 cc. concentrated H2SO4 to 90 g. I in 200 cc. Et2O, warming the mixture 0.5 hr. at 15°, and diluting it after several hrs. with 3-4 fold ice-H2O give up to 85% DL-styrylglycolic acid (II) amide, m. 141°, which (10 g.), refluxed 1 hr. with 15 g. (CO2H)2 in 200 cc. H2O, gives 80% II, m. 137°. Concentrating slowly in vacuo a mixture of 30 g. (+)-bornylamine (III) in 200 cc. Et2O and 30 g. II in 200 cc. MeOH until 2/3 of the solvents are evaporated, filtering off the precipitate; [α]D 18°, and recrystg. it 7-8 times from Me2CHOH give 20 g. III D-styrylglycolate, [α]D 28° (MeOH). Recrystg. the residue of the original mother liquor several times from H2O gives 10 g. III L-styrylglycolate, [α]D -6°. Decomposition of the salts gives D-II, m. 139° (decomposition), [α]D 100° (MeOH), and L-II (-)-isomer, m. 139°, [α]D -98°. Hydrogenation of D-II in MeOH 5 min. with PtO2 gives 100% (+)-α-hydroxy-γ-phenylbutyric acid (IV), m. 114-15°, [α]D20 10.4° (EtOH). Refluxing 4.5 g. IV in 135 cc. absolute MeOH 16 hrs. with 5 cc. concentrated H2SO4 gives 4 g. Me ester (V), b16 155-7°, [α]D20 23° (C6H6). Shaking 3 g. V 6 hrs. with 50 cc. supersatd. NH3-NH4OH gives the amide (VI), needles, m. 124°, [α]D20 -37° (MeOH); DL-amide, m. 130°. Bromination of D-II in CHCl3 gives (-)-α-hydroxy-β,γ-dibromo-γ-phenylbutyric acid (VII), m. 177° (decomposition), [α]D20 -60° (MeOH). Condensation of 36 g. m-O2NC6H4CH:CHCHO in 300 cc. CHCl3 with 42 g. NaCN and 22 cc. 35.4% HCl as above gives 70-80% (3-nitrostyryl)glycolic acid (VIII) nitrile (IX), m. 76-8°, which, treated with BzCl and C5H5N, gives the O-Bz derivative, m. 111°. Treating 32 g. IX in 200 cc. Et2O with 79 cc. concentrated HCl and 12.6 cc. concentrated H2SO4 3 days at 20°, pouring the mixture into ice-H2O, extracting with Et2O, and recrystg. the residue of the Et2O extract give 20-22 g. VIII, slightly yellow needles, m. 130-5° (decomposition), which, treated with Br in CHCl3, gives α-hydroxy-β,γ-dibromo-γ-(3-nitrophenyl)butyric acid, m. 175-6° (decomposition). Resolution of VIII with III gives a III (+)-VIII salt, [α]D20 24° (MeOH), from which the free (+)-VIII, m. 112-17°, [α]D20 71°, is obtained on decomposition with HCl. Hydrogenation of (+)-VIII in MeOH with PtO2 gives (+)-α-hydroxy-γ-(3-aminophenyl)butyric acid (not quite pure), [α]D20 0.75° (MeOH), which, diazotized and treated with Cu2H2, gives (+)-α-hydroxy-γ-phenylbutyric

L6 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

acid, m. 113°, [α]D20 10.6°. Hydrogenation of 20 g. β-phenylglycidic acid Et ester in 50 cc. EtOH with 2 g. Raney Ni 8 hrs. at 20° and atm. pressure gives PhCH2CH(OH)CO2Et, b16 153°, which, sapond. with NaOEt, gives the free acid, m. 96° (Ac deriv., m. 72°; amide, m. 112°). The equil. consts. of the m- and p-substituted PhCOMe are detd. to be, resp.: NO2, 0.43, 0.28; Br, 0.77, 1.2; MeO, 1.27, 7.4; NHAc, 1.31, 6; Me, 1.53, 3; OH, 1.47, 14; H, 1.52, 1.52; NH2, 1.73, 18; PhCH:CHCHO, 0.032; 3-NO2 analog, 0.023; 3-O2NC6H4COMe, 0.43. The rotation dispersions of D-II, VI, VII, and VIII in MeOH, EtOH, dioxane, Me2CO, AcOH, and NaOH are given in tables.

IT **7226-82-6**, Butyric acid, 2-hydroxy-4-phenyl-, methyl ester
(preparation of)

RN 7226-82-6 CAPLUS
CN Benzenebutanoic acid, α-hydroxy-, methyl ester (9CI) (CA INDEX NAME)



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         25916 NITRILES
         70084 NITRILE
                 (NITRILE OR NITRILES)
L7           7 L5 AND NITRILE

=> d ibib abs hitstr tot
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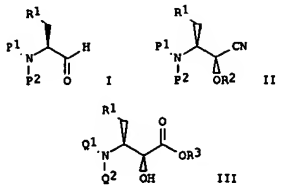
L7 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:700272 CAPLUS
DOCUMENT NUMBER: 141:174475
TITLE: Process for producing erythro-3-amino-2-hydroxybutyric acid derivatives
INVENTOR(S): Furukawa, Yoshiro; Yaegashi, Keisuke; Hinoue, Kazumasa
PATENT ASSIGNEE(S): Daiso Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1449824	A1	20040825	EP 2004-290653	20000622
R: CH, DE, FR, GB, LI				
EP 1063232	A2	20001227	EP 2000-401792	20000622
EP 1063232	A3	20010307		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: JP 1999-174967 A 19990622
EP 2000-401792 A3 20000622
OTHER SOURCE(S): CASREACT 141:174475; MARPAT 141:174475
GI



AB A process for producing an erythro-3-amino-2-hydroxybutyric acid derivative involves reaction of a 2-amino aldehyde derivative I [R1 is alkyl, cycloalkyl, alkylthio, arylthio or (un)substituted aryl; P1, P2 are (un)substituted aralkyl, alkyloxycarbonyl, arylcarbonyl or arylsulfonyl] with a metal cyanide in the presence of an acid chloride and/or an acid anhydride to give stereoselectively an erythro-3-amino-2-hydroxybutyronitrile derivative II [same R1, P1 and P2; R2 is alkylcarbonyl or (un)substituted arylcarbonyl group]. The nitrile derivative II is treated with an acid in water or aqueous solvent to convert it into an erythro-3-amino-2-hydroxybutyric acid derivative III [same R1; R3 is H; Q1, Q2 are H, (un)substituted aralkyl or arylsulfonyl] or with an acid in an alc. solvent R3OH to convert it into an ester III [same R1, Q1 and Q2; R3 is alkyl, cycloalkyl or (un)substituted aralkyl] under two-phase catalysis. Thus, the process was applied to the synthesis of Me

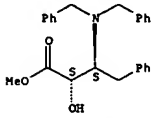
L7 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

(2S,3S)-3-(dibenzylamino)-2-hydroxy-4-phenylbutyrate (erythro:threo = 97:13, 73% yield) starting from N,N-dibenzyl-L-phenylalaninal.

IT 189562-45-6P 313468-87-0P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(production of aminohydroxybutyric acid derivs.)

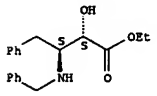
RN 189562-45-6 CAPLUS
CN Benzenebutanoic acid, β-[bis(phenylmethyl)amino]-α-hydroxy-, methyl ester, (αS,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 313468-87-0 CAPLUS
CN Benzenebutanoic acid, α-hydroxy-β-[(phenylmethyl)amino]-, ethyl ester, (αS,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

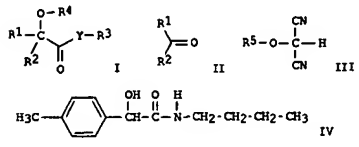


L7 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:444539 CAPLUS
DOCUMENT NUMBER: 137:33079
TITLE: Process for preparation of α-hydroxy amides and related α-hydroxy carbonyl compounds by, e.g., condensation of carbonyl compds., (silyloxy)propanedinitriles, and amines.
INVENTOR(S): Nemoto, Hisao
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: U.S., 34 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6403818	B1	20020611	US 2001-794140	20010228

PRIORITY APPLN. INFO.: US 2000-185399P P 20000228
OTHER SOURCE(S): CASREACT 137:33079; MARPAT 137:33079
GI



AB A novel process is disclosed for the one-pot preparation of α-hydroxy carbonyl compds. (mostly α-hydroxy amides) of formula I and their derivs. via the condensation of II and III in the presence of R3-YH [wherein: Y = O, S, NR6 (R6 = H, OH, alkyl, alkoxy, cycloalkyl, alkenyl, alkynyl, or (un)substituted 5- to 12-membered heteroaryl group, etc.); R1, R2 independently = H, alkyl, alkoxy, cycloalkyl, bicycloalkyl, alkenyl, alkynyl, heteroaryl or (un)substituted 5- to 12-membered heteroaryl group, etc.; R3 = H, OH, alkyl, alkoxy, cycloalkyl, alkenyl, alkynyl, aryl, (un)substituted 5 to 12-membered heteroaryl group, etc.; R4 = H, substituted silyl protecting group (preferably -SiMe3, -SiMe2tBu or SiPh2tBu), alkanoyl, alkenoyl, alkynoylaryloyl, heteroaryloyl, etc.; R5 = substituted silyl protecting group (preferably -TMS, -TBDMS or -TBDPS), alkanoyl, alkenoyl, alkynoyl, aryloyl, heteroaryloyl, etc.]. A key intermediate in the proposed process is the corresponding acyl cyanide, generated in situ from condensation of II and III. For example, to a stirred solution of 4-methylbenzaldehyde (1.0 mmol) and dinitrile III (R4 = tert-butyldimethylsilyl, 1.2 mmol) in acetonitrile (3 mL) at 0° was added n-butylamine (1.1 mmol) in one portion. After 5 min, a solution of tetrabutylammonium fluoride in THF (1.5 mmol) was added dropwise and the reaction stirred at 0° for an addnl. 20 min. The solution was concentrated and purified via silica gel column chromatog. to provide hydroxyacetamide IV as colorless powder in 94% yield. Approx. 75 specific examples of I were prepared The invention is proposed to be useful for the production of

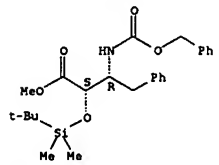
L7 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

statine analogs. The invention process gives products similar to the Passerini reaction, but uses amines instead of isocyanides, and also gives higher yields.

IT 342389-98-4P 342390-00-5P 435344-70-0P, Methyl 2-[(tert-butyldimethylsilyl)oxy]-4-phenylbutanoate
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(product; preparation of α-hydroxy carbonyl derivs. and related compds. by condensation of carbonyl compds., (silyloxy)propanedinitriles, and amines)

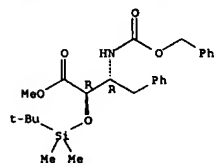
RN 342389-98-4 CAPLUS
CN Benzenebutanoic acid, α-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-β-[[(phenylmethoxy)carbonyl]amino]-, methyl ester, (αR,βS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



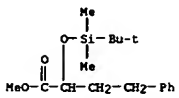
RN 342390-00-5 CAPLUS
CN Benzenebutanoic acid, α-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-β-[[(phenylmethoxy)carbonyl]amino]-, methyl ester, (αR,βR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



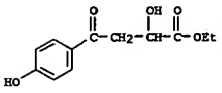
RN 435344-70-0 CAPLUS
CN Benzenebutanoic acid, α-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)

L7 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:228191 CAPLUS
DOCUMENT NUMBER: 122:81272
TITLE: Nitrile oxide [3 + 2] cycloaddition: application to the synthesis of 6-substituted 3(2H)-pyridazinones and 6-substituted 4,5-dihydro-4-hydroxy-3(2H)-pyridazinones
AUTHOR(S): Baraldi, P. G.; Bigoni, A.; Cacciari, B.; Caldari, C.; Manfredini, S.; Spalluto, G.
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Univ. di Ferrara, Ferrara, I-44100, Italy
SOURCE: Synthesis (1994), (11), 1158-62
CODEN: SYNTBF; ISSN: 0039-7881
PUBLISHER: Thieme
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 122:81272
AB An efficient method for the preparation of 6-substituted 3(2H)-pyridazinones and 6-substituted 4,5-dihydro-4-hydroxy-3(2H)-pyridazinones starting from 3,5-disubstituted 4,5-dihydroisoxazoles is described. N-O bond cleavage of the isoxazoline ring promoted by molybdenum hexacarbonyl or by catalytic hydrogenation afforded the α-hydroxy γ-keto esters RCOCH2CH(OH)CO2Et (I, R = Me, Bu, 2-, 4-pyridyl, 4-HOC6H4) which were converted into 6-substituted 4,5-dihydro-4-hydroxy-3(2H)-pyridazinones for 6-substituted 3(2H)-pyridazinones on treatment with hydrazine hydrate at room temperature or reflux in high yield starting from I. An intramol. version of this methodol. has been developed to prepare the known antiulcer tricyclic 5H-[1]-benzopyrano[4,3-c]pyridazin-3(2H)-one.
IT 160427-19-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(nitrile oxide [3 + 2] cycloaddn. to pyridazinones)
RN 160427-19-0 CAPLUS
CN Benzenebutanoic acid, α,4-dihydroxy-γ-oxo-, ethyl ester (9CI) (CA INDEX NAME)

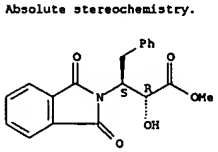


L7 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:560824 CAPLUS
DOCUMENT NUMBER: 119:160824
TITLE: Process for the preparation of α-hydroxy-β-aminocarboxylic acids
INVENTOR(S): Baenziger, Markus; Warm, Aleksander; McGarrity, John
PATENT ASSIGNEE(S): Lonza A.-G., Switz.
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 543343	A2	19930526	EP 1992-119634	19921117
EP 543343	A3	19930721		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
JP 06184069	A2	19940705	JP 1992-303629	19921113
CA 2083108	AA	19930520	CA 1992-2083108	19921117
PRIORITY APPLN. INFO.:			CH 1991-3373	A 19911119

OTHER SOURCE(S): CASREACT 119:160824; MARPAT 119:160824
AB R1CH(NR3R4)CH(OH)CO2R2 [R1 = (substituted) alkyl; R2 = H, alkyl; R3, R4 = H, protecting group; R3R4 = bifunctional protecting group], were prepared by 1) treatment of R1CH(NR5R6)COX (R5,R6 = R3,R4, except that both R5,R6 cannot = H; X = Br, Cl) with Me3SiCN to give R1CH(NR5R6)COCN, 2) conversion of the nitrile to R1CH(NR5R6)COCO2R7 (R7 = alkyl), 3) selective reduction of the keto group, and 4) optional deprotection/ester hydrolysis. Thus, N-phthaloyl-L-phenylalanine was refluxed with SOCl2 to give 98% acid chloride, which was heated with Me3SICN and ZnI2 in 7HF to give 87% nitrile. This in Et2O/MeOH/HCl was stirred at -10° followed by addition of H2O to give 68% Me S-2-oxo-4-phenyl-3-phthalimidobutyrate. The latter was reduced with LiBH4 in THF at -25° to give 96% Me (2R,3S)- and (2S,3S)-2-hydroxy-4-phenyl-3-phthalimidobutyrate. This was converted to cyclohexylnorstatine hydrochloride.
IT 150095-77-5P 150095-78-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for α-hydroxy-β-aminocarboxylic acid derivative)
RN 150095-77-5 CAPLUS
CN 2H-Isoindole-2-propanoic acid, 1,3-dihydro-α-hydroxy-1,3-dioxo-β-(phenylmethyl)-, methyl ester, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

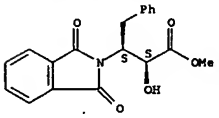
Absolute stereochemistry.



RN 150095-78-6 CAPLUS
CN 2H-Isoindole-2-propanoic acid, 1,3-dihydro-α-hydroxy-1,3-dioxo-β-(phenylmethyl)-, methyl ester, (αS,βS)- (9CI) (CA INDEX NAME)

L7 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

Absolute stereochemistry.



L7 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

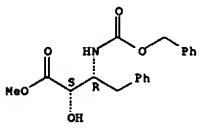
ACCESSION NUMBER: 1992:651744 CAPLUS
DOCUMENT NUMBER: 117:251744
TITLE: Aminodeoxybestatin and epi-aminodeoxybestatin: stereospecific synthesis and aminopeptidase inhibition
AUTHOR(S): Herranz, Rosario; Vinuesa, Soledad; Castro-Pichel, Julia; Perez, Concepcion; Garcia-Lopez, M. Teresa
CORPORATE SOURCE: Inst. Quim. Med., CSIC, Madrid, 28006, Spain
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1992), (14), 1825-30
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 117:251744

AB The synthesis of (2S,3R)-DAPBA-L-Leu-OH (DAPBA = 2,3-diamino-4-phenylbutanoic acid) (aminodeoxybestatin) and (2R,3R)-DAPBA-L-Leu-OH (epi-aminodeoxybestatin), bestatin and epi-bestatin analogs, resp., in which the hydroxy group has been replaced with an amino group, is described by two different methods. The first one involves the synthesis of bis-(N-Z)-DAPBA (Z = benzyloxycarbonyl), by homologation of N-Z-phenylalanine, via a modified Strecker synthesis followed by subsequent coupling with the Me ester of L-leucine and removal of the protecting groups. Following this procedure, 25% racemization at the C-3 center of the DAPBA derivs. took place during the homologation reaction. The second method involves the stereospecific SN2 nucleophilic substitution of the 2-hydroxy group of (2R,3R)- and (2S,3R)-3-(benzyloxycarbonyl)amino-2-hydroxy-4-phenylbutanoyl-L-leucine Me esters, and subsequent saponification, azido reduction and removal of the N-Z-protecting group. Replacement of the hydroxy group of bestatin and epi-bestatin with an amino group results in a decrease in their aminopeptidase (AP-B, AP-M and Leu-AP)-inhibitory potencies.

IT 124782-04-3P 124782-06-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and mesylation of)

RN 124782-04-3 CAPLUS
CN Benzenebutanoic acid, α-hydroxy-β-[[(phenylmethoxy)carbonyl]amino]-, methyl ester, (αS,βR)- (9CI) (CA INDEX NAME)

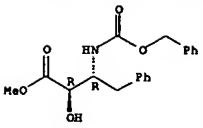
Absolute stereochemistry. Rotation (+).



RN 124782-06-5 CAPLUS
CN Benzenebutanoic acid, α-hydroxy-β-[[(phenylmethoxy)carbonyl]amino]-, methyl ester, (αR,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

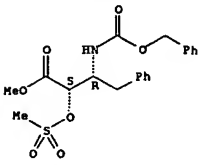
L7 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



IT 144676-50-6P 144676-51-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and substitution reaction of, with azide)

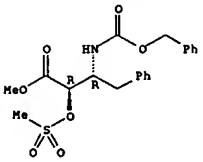
RN 144676-50-6 CAPLUS
CN Benzenebutanoic acid, α-[(methylsulfonyl)oxy]-β-[[(phenylmethoxy)carbonyl]amino]-, methyl ester, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



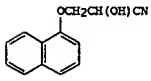
RN 144676-51-7 CAPLUS
CN Benzenebutanoic acid, α-[(methylsulfonyl)oxy]-β-[[(phenylmethoxy)carbonyl]amino]-, methyl ester, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1989:594247 CAPLUS
DOCUMENT NUMBER: 111:194247
TITLE: Lipase-catalyzed irreversible transesterification using enol esters: resolution of cyanohydrins and syntheses of ethyl (R)-2-hydroxy-4-phenylbutyrate and (S)-propranolol
AUTHOR(S): Wang, Yi Fong; Chen, Shui Tein; Liu, Kevin K. C.; Wong, Chi Huey
CORPORATE SOURCE: Dep. Chem., Texas A and M Univ., College Station, TX, 77843, USA
SOURCE: Tetrahedron Letters (1989), 30(15), 1917-20
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 111:194247
GI



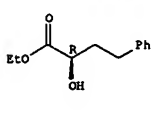
I

AB Racemic hydroxyacetonitriles, (±)-I, (±)-PhCH2CH2CH(OH)CN, and (±)-PhCH2OCH2CH(OH)CN, were resolved by lipoprotein lipase. (±)-I gave (+)-I which was sequentially reduced (LiAlH4) and treated with Me2CO and NaBH4 to give (S)-propranolol.

IT 90315-82-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 90315-82-5 CAPLUS
CN Benzenebutanoic acid, α-hydroxy-, ethyl ester, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L7 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1957:1600 CAPLUS
DOCUMENT NUMBER: 51:1600
ORIGINAL REFERENCE NO.: 51:287d-i,288a-b
TITLE: The synthesis of mandelic acid analogs. II. Styrylglycolic acids
AUTHOR(S): Nerdel, Friedrich; Rachel, Hans
CORPORATE SOURCE: Tech. Univ., Berlin-Charlottenburg
SOURCE: Chemische Berichte (1956), 89, 671-7
CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 51:1600

AB cf. C.A. 49, 6217e. Adding dropwise 54 cc. concentrated HCl to 80 cc. PhCH:CHCHO and 49 g. NaCN in 250 cc. Et2O cooled with ice, stirring the mixture 1 hr. at 0° and 1 hr. at 20°, washing the filtered Et2O solution with concentrated NaHSO3 and recrystg. the residue from CS2 give 65-70% DL-PhCH:CHCH(OH)CN (I), m. 74-5°. Adding dropwise at below 10° a mixture of 250 cc. concentrated HCl and 40 cc. concentrated H2SO4 to 90 g. I in 200 cc. Et2O, warming the mixture 0.5 hr. at 15°, and diluting it after several hrs. with 3-4 fold ice-H2O give up to 85% DL-styrylglycolic acid (II) amide, m. 141°, which (10 g.), refluxed 1 hr. with 15 g. (CO2H)2 in 200 cc. H2O, gives 80% II, m. 137°. Concentrating slowly in vacuo a mixture of 30 g. (+)-bornylamine (III) in 200 cc. Et2O and 30 g. II in 200 cc. MeOH until 2/3 of the solvents are evaporated, filtering off the precipitate, [α]D 18°, and recrystg. it 7-8 times from Me2CHOH give 20 g. III D-styrylglycolate, [α]D 28° (MeOH). Recrystg. the residue of the original mother liquor several times from H2O gives 10 g. III L-styrylglycolate, [α]D -6°. Decomposition of the salts gives D-II, m. 139° (decomposition), [α]D 100° (MeOH), and L-II (-)-isomer, m. 139°, [α]D -98°. Hydrogenation of D-II in MeOH 5 min. with PtO2 gives 100% (+)-α-hydroxy-γ-phenylbutyric acid (IV), m. 114-15°, [α]D20 10.4° (EtOH). Refluxing 4.5 g. IV in 135 cc. absolute MeOH 16 hrs. with 5 cc. concentrated H2SO4 gives 4 g. Me ester (V), b16 155-7°, [α]D20 23° (C6H6). Shaking 3 g. V 6 hrs. with 50 cc. supersatd. NH3-NH4OH gives the amide (VI), needles, m. 124°, [α]D20 -37° (MeOH); DL-amide, m. 130°. Bromination of D-II in CHCl3 gives (-)-α-hydroxy-β,γ-dibromo-γ-phenylbutyric acid (VII), m. 177° (decomposition), [α]D20 -60° (MeOH). Condensation of 36 g. m-O2NC6H4CH:CHCHO in 300 cc. CHCl3 with 42 g. NaCN and 22 cc. 35.4% HCl as above gives 70-80% (3-nitrostyryl)glycolic acid (VIII) nitrile (IX), m. 76-8°, which, treated with BzCl and C5H5N, gives the O-Bz derivative, m. 111°. Treating 32 g. IX in 200 cc. Et2O with 79 cc. concentrated HCl and 12.6 cc. concentrated H2SO4 3 days at 20°, pouring the mixture into ice-H2O, extracting with Et2O, and recrystg. the residue of the Et2O extract give 20-22 g. VIII, slightly yellow needles, m. 130-5° (decomposition), which, treated with Br in CHCl3, gives α-hydroxy-β,γ-dibromo-γ-(3-nitrophenyl)butyric acid, m. 175-6° (decomposition). Resolution of VIII with III gives a III (+)-VIII salt, [α]D20 24° (MeOH), from which the free (+)-VIII, m. 112-17°, [α]D20 71°, is obtained on decomposition with HCl. Hydrogenation of (+)-VIII in MeOH with PtO2 gives (+)-α-hydroxy-γ-(3-aminophenyl)butyric acid (not quite pure), [α]D20 0.75° (MeOH), which, diazotized and treated with Cu2H2, gives (+)-α-hydroxy-γ-phenylbutyric acid, m. 113°, [α]D20 10.6°. Hydrogenation of 20 g. β-phenylglycidic acid Et ester in 50 cc. EtOH with 2 g. Raney Ni 8

L7 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
hrs. at 20° and atm. pressure gives PhCH2CH(OH)CO2Et, b16 153°, which, sapond. with NaOEt, gives the free acid, m. 96° (Ac deriv., m. 72°; amide, m. 112°). The equil. consts. of the m- and p-substituted PhCOMe are detd. to be, resp.: NO2, 0.43, 0.28; Br, 0.77, 1.2; MeO, 1.27, 7.4; NHAc, 1.31, 6; Me, 1.53, 3; OH, 1.47, 14; H, 1.52, 1.52; NH2, 1.73, 18; PhCH:CHCHO, 0.032; 3-NO2 analog, 0.023; 3-O2NC6H4COMe, 0.43. The rotation dispersions of D-II, VI, VII, and VIII in MeOH, EtOH, dioxane, Me2CO, AcOH, and NaOH are given in tables.

IT 7226-82-6, Butyric acid, 2-hydroxy-4-phenyl-, methyl ester
(preparation of)

RN 7226-82-6 CAPLUS

CN Benzenebutanoic acid, α-hydroxy-, methyl ester (9CI) (CA INDEX NAME)